Patents

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Application of:	)	
	)	
AGOSTON ET AL.	)	
	)	Art Unit: **1616**
Serial No.: **09/644,387**	)	
	)	Examiner: **Badio, B.**
Filed: **August 23, 2000**	)	
	)	
For: **METHODS OF OBTAINING 2-METHOXYESTRADIOL OF HIGH PURITY**	)	

APPENDIX

Claims For Appeal:

1. A pharmaceutical composition being substantially free of steroid contaminants having estrogenic or carcinogenic effects comprising 2-methoxyestradiol having a purity greater than 99.5% as determined by HPLC.

2. The composition of Claim 1, containing less than 0.03% estradiol and less than 0.02% estrone.

3. The composition of Claim 2, containing less than 0.01% estradiol and less than 0.01% estrone.

4. The composition of Claim 2, further containing less than 0.02% 2-hydroxyestradiol.

5. The composition of Claim 2, further containing less than 0.02% 4-hydroxyestradiol.

6. The composition of Claim 2, further containing less than 0.02% 4-methoxyestradiol.

7. The composition of Claim 1, containing 0.01% or less estradiol, 0.02% or less 2-hydroxyestradiol, 0.01% or less 4-hydroxyestradiol, 0.01% or less 4-methoxyestradiol and 0.01% or less estrone.

8. A pharmaceutical composition being substantially free of steroid contaminants having estrogenic or carcinogenic effects comprising 2-methoxyestradiol having a purity greater than 98.0% and containing less than 0.03% estradiol and less than 0.02% estrone.

9. The composition of Claim 8, containing less than 0.01% estradiol and less than 0.01% estrone.

10. The composition of Claim 8, containing 0.01% or less estradiol, 0.02% or less 2-hydroxyestradiol, 0.01% or less 4-hydroxyestradiol, 0.01% or less 4-methoxyestradiol and 0.01% or less estrone.

11. The composition of Claim 8, wherein the 2-methoxyestradiol has a purity greater than 99.0%.

12. The composition of Claim 11, containing less than 0.01% estradiol and less than 0.01% estrone.

13. The composition of Claim 11, containing 0.01% or less estradiol, 0.02% or less 2-hydroxyestradiol, 0.01% or less 4-hydroxyestradiol, 0.01% or less 4-methoxyestradiol and 0.01% or less estrone.

21. A pharmaceutical composition being substantially free of steroid contaminants having estrogenic or carcinogenic effects comprising 2-methoxyestradiol having a purity greater than 98% and containing less than 0.03% estradiol and less than 0.02% estrone produced by the process comprising:

protecting the 3- and 17-hydroxyl groups of estradiol;

reacting the protected estradiol with bromine and acetic acid to produce a 2-brominated derivative of estradiol;

reacting the 2-brominated derivative of estradiol with sodium methoxide in the presence of a copper catalyst;

removing the protecting groups on the 3- and 17-hydroxyl groups to produce 2-methoxyestradiol; and

purifying the 2-methoxyestradiol using liquid chromatography on an adsorption/partition medium with a solvent system comprising a polar and a nonpolar solvent.

22. A pharmaceutical composition being substantially free of steroid contaminants having estrogenic or carcinogenic effects comprising 2-methoxyestradiol having a purity greater than 98% and containing less than 0.03% estradiol and less than 0.02% estrone produced by the process comprising:

ring-brominating estradiol by reacting estradiol with bromine in the presence of acetic acid to produce a ring-brominated intermediate;

reacting the ring-brominated intermediate with sodium methoxide in the presence of a copper catalyst to produce 2-methoxyestradiol; and

purifying the 2-methoxyestradiol using liquid chromatography on an adsorption/partition medium with a solvent system comprising a polar and a nonpolar solvent.

23. A pharmaceutical composition being substantially free of steroid contaminants having estrogenic or carcinogenic effects comprising 2-methoxyestradiol having a purity greater than 98% and containing less than 0.03% estradiol and less than 0.02% estrone produced by the process comprising:

protecting the 3- and 17-hydroxyl groups of estradiol;

reacting the protected estradiol with nitric acid and acetic acid to produce a 2-nitro derivative of estradiol;

reducing the 2-nitro derivative of estradiol to produce the corresponding 2-amino derivative of estradiol;

reacting the 2-amino derivative of estradiol under Sandmeyer conditions to produce a 3-,17-hydroxyl protected 2-methoxyestradiol; and

removing the protecting groups on the 3- and 17-hydroxyl groups to produce 2-methoxyestradiol.

24. A pharmaceutical composition being substantially free of steroid contaminants having estrogenic or carcinogenic effects comprising 2-methoxyestradiol having a purity greater than 98% and containing less than 0.03% estradiol and less than 0.02% estrone produced by the process comprising:

protecting the 3-hydroxyl group of estrone;

reacting the protected estrone with nitric acid and acetic acid to produce a 2-nitro derivative of estrone;

reducing the 2-nitro derivative of estrone to produce the corresponding 2-amino derivative of estrone;

reacting the 2-amino derivative of estrone under Sandmeyer conditions to produce a 3-hydroxyl protected 2-methoxyestrone;

removing the protecting group on the 3-hydroxyl group to produce 2-methoxyestrone; and

reducing the 17-keto group of 2-methoxyestrone to produce 2-methoxyestradiol.

25. A pharmaceutical composition being substantially free of steroid contaminants having estrogenic or carcinogenic effects comprising 2-methoxyestradiol having a purity greater than 98% and containing less than 0.03% estradiol and less than 0.02% estrone produced by the process comprising:

brominating estradiol in the presence of acetic acid to produce a mixture of ring-brominated estradiols;

isolating 2-bromoestradiol from the mixture of estradiols; and

reacting the 2-bromoestradiol with sodium methoxide in the presence of a copper catalyst to produce 2-methoxyestradiol.